Health Canada / Santé Canada

Volume 6, Number 4
October 1996

Canadian Adverse Drug Reaction Newsletter

Drugs Directorate

IN THIS ISSUE:
Cefaclor-associated serum sickness-like reaction
Newsletter Assessment - Questionnaire

Cefaclor-associated serum sickness-like reaction

Serum sickness was first described by von Pirquet in 1905 following the use of antidiptheria horse serum.[1] It is characterized by fever, arthralgia, skin eruptions, lymphadenopathy, nephritis, edema and neuritis.[2]

A similar condition, known as serum sickness-like reaction (SSLR), has been recognized in association with a variety of drugs including: penicillin, sulfonamides, thiouracils, hydantoins, *p*-aminosalicylic acid, phenylbutazone, thiazides and streptomycin.[3] Cases of SSLR have also been reported following the use of cefaclor, a second generation cephalosporin. In contrast to classic serum sickness, signs and symptoms of SSLR involving cefaclor appear to be confined primarily to findings including erythema multiforme or other skin manifestations accompanied by arthritis or arthralgia, with or without fever.[4,5]

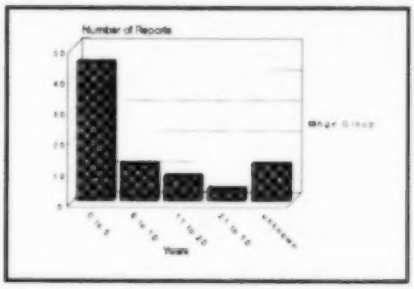
Cefaclor (Ceclor™) was approved for use in Canada in November 1979 for the treatment of otitis media, lower and upper respiratory tract infections, urinary tract infections and skin and soft-tissue infections.

A review of the Canadian national adverse drug reaction (ADR) database was performed for reports associated with the use of cefaclor in which the reporter had "diagnosed" and reported the reaction as SSLR. Eighty-one cases (41 women, 34 men, 6 not stated) were retrieved over a 16-year time period.

Many of the case reports described the skin rashes and joint complaints associated with the SSLR. Of particular concern was one case that stated an 8-year-old boy was unable to walk due to the pain in his legs.

As reported in the product monograph[4] and various literature articles,[1,5,6] SSLR associated with cefaclor appears to occur more frequently in children. As shown in Figure 1, 55.6% (45/81) of the cases retrieved from the Canadian national ADR database involved children less than 6 years of age. However, this may merely reflect the extensive use of this antibiotic in this age group.

Figure 1: Serum sickness-like reaction (SSLR) associated with the use of cefaclor: Distribution by age group



SSLR generally occurs during or following a second or subsequent course of therapy with cefaclor. The clinical manifestations usually begin approximately seven days into the course of therapy, with a range of 0 to 20 days. Of the case reports that provided information on the time to onset of the reaction, 61.5% (32/52) reported the onset time to be between 7 and 15 days. Those cases with an onset time before 7 days may indicate there was a prior exposure to the drug. Unfortunately, very few reports provided information on the patient's drug history.

SSLR appears to cause little sustained morbidity. Of the cases that reported information on the outcome of the patient: 24 patients recovered, 1 had not yet recovered at the time of reporting, 1 had recovered with residual effects, and one case of SSLR was reported in a 15-month old infant with Down's syndrome who had unresolved pneumonia and subsequently died. Occasionally SSLR has resulted in hospitalization, usually of short duration. Of the 81 cases retrieved from the Canadian national ADR database, 21 reported hospitalization or an emergency room visit.

Drug-induced SSLR usually abates within days after withdrawal of the causative agent. However, symptomatic therapy may include antihistaminic drugs, analgesics and, in severe cases, glucocorticoids.[3,4]

While SSLR is appropriately described in the product monograph, the wide use of cefaclor has prompted the Canadian Adverse Drug Reaction Monitoring Program to remind health care professionals of the occurrence of this reaction, particularly in young patients. Furthermore, knowledge of the family's drug history may be pertinent as one study suggests cefaclor-associated SSLR may result from inherited defects in the metabolism of reactive intermediates.[7]

References

1. Vial T, Pont J, Pham E, Rabilloud M, Descotes J: Cefaclor-associated serum sickness-like disease: Eight cases and review of the literature. *Ann Pharmacother* 1992;26:910-4
2. Parker CW: Drug allergy. *N Engl J Med* 1975;292:511-4
3. Isselbacher KJ, Braunwald E, Wilson JD et al, editors. Harrison's Principles of Internal Medicine, *13th ed.* New York: McGraw Hill, 1994: 280, 406-7, 1635, 1639, 1641, 1674
4. Drug Product Monograph, Copyright 1995, Eli Lilly Canada Inc.
5. Hebert AA, Sigman ES, Levy ML: Serum sickness-like reactions from cefaclor in children. *J Am Acad Dermatol* 1991;25:805-8
6. Martin J, Abbott G: Serum sickness like illness and antimicrobials in children. *N Zealand Med J* 1995;108:123-4
7. Kearns GL, Wheeler, JG, Childress SH, Letzig LG: Serum sickness-like reactions to cefaclor: Role of hepatic metabolism and individual susceptibility. *J Pediatr* 1994;125:805-11

Please Note: A voluntary reporting system thrives on intuition, lateral thinking and openmindedness. For these reasons, most adverse drug reactions (ADR) can only be considered to be *suspicions*, for which a proven causal association has not been established. Due to the fact that there is gross underreporting of ADRs and that a definite causal association cannot be determined, this information cannot be used to estimate the incidence of adverse reactions.

ADRs are nevertheless invaluable as a source of potential new and undocumented *signals*.

Canada The Canadian Adverse Drug Reaction Monitoring Newsletter is prepared and funded by the Drugs Directorate, Health Canada and published in the CMAJ regularly.

CANADIAN ADVERSE DRUG REACTION (ADR) NEWSLETTER ASSESSMENT

The Canadian Adverse Drug Reaction Monitoring Program (CADRMP) created the Canadian ADR Newsletter in 1991, and since 1994 it has been published on a quarterly basis.

As the CADRMP aims to publish a newsletter that is useful for health professionals, we would like to seek your comments.

Please complete the short questionnaire at your earliest convenience and return it to us by mail (address on reverse side of questionnaire) OR fax at (613) 957-0335.

Thanking you in advance for your cooperation. Please be assured that a few minutes of your time will contribute to improve future issues of the Canadian ADR Newsletter.

Canadian Adverse Drug Reaction (ADR) Newsletter Questionnaire

		Yes	No
Q1.	a) Do you find the Newsletter professionally relevant?	Y	N
	b) Do you find the means of distribution of the Newsletter satisfactory?	Y	N
	c) Do you find the length of the Newsletter adequate?	Y	N

Please make any additional comments regarding the above questions here.

Q2. Using the scale below, please rate your level of interest in the content of the Newsletter by circling the appropriate score.

1. High 2. Moderate 3. Low 4. None

In terms of:

a)	Articles on ADRs for new drugs (< 5 years on market)	1. 2. 3. 4.
b)	Articles on ADRs for older drugs	1. 2. 3. 4.
c)	Articles on ADRs for an individual drug	1. 2. 3. 4.
d)	Articles on ADRs for a class of drugs	1. 2. 3. 4.
e)	Presentation of specific reactions	1. 2. 3. 4.
f)	Presentation of ADR profile	1. 2. 3. 4.
g)	List of drugs of current interest	1. 2. 3. 4.
h)	Changes in labelling of ADRs in product monographs	1. 2. 3. 4.
i)	Information on international safety issues	1. 2. 3. 4.
j)	Specific topics (e.g., annual statistics; elderly; switches to over-the-counter)	1. 2. 3. 4.
k)	Annual index of topics in the Newsletter	1. 2. 3. 4.
l)	Including ADR reporting form in the Newsletter	1. 2. 3. 4.
m)	Editorials about the ADR Monitoring Program	1. 2. 3. 4.

Other: **Please make any comments regarding the above statements and suggestions for other topics in the space below or on the reverse.**

Q3. Presently, the Newsletter is published quarterly. Should this be changed? Yes (Y) No (N)

If yes, what frequency of publication would you suggest? _____

Q4. Information about you: please tick all those that apply or complete where indicated.

Physician _____ Community _____ Province (specify) _____

Pharmacist _____ Institution _____ Specialty (specify) _____

Nurse _____ Manufacturer _____

Other (specify) _____ Other (specify) _____

Thank you for taking the time to complete this questionnaire. Please return it to us by mail (address on reverse) OR fax at (613) 957-0335. Please feel free to make photocopies of this form and distribute them to colleagues who read the *Newsletter*.

ADR Reporting Section
Continuing Assessment Division
Bureau of Drug Surveillance
Drugs Directorate / Health Protection Branch
Address Locator #4103B1
Ottawa, Ontario
K1A 1B9

Fold here _____

Additional comments _____